UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

PORTAL INSTRUMENTS, INC.,

Plaintiff,

v.

LEO PHARMA A/S,

Defendant.

Case No. 22 Civ. 9156 (JHR)

DEFENDANT'S OPPOSITION TO PLAINTIFF'S MOTION TO EXCLUDE TESTIMONY OF UMESH BANAKAR

COVINGTON & BURLING LLP
Mark P. Gimbel
Jordan S. Joachim
The New York Times Building
620 Eighth Avenue
New York, New York 10018
212-841-1000
mgimbel@cov.com
jjoachim@cov.com

Attorneys for Defendant LEO Pharma A/S

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases

Other Authorities

Defendant LEO Pharma A/S ("LEO") respectfully submits this opposition to the Motion to Exclude Testimony of Umesh Banakar filed by Portal Instruments, Inc. ("Portal").

PRELIMINARY STATEMENT

Portal's remaining claims in this action assert that LEO is obligated to pay a $1 million milestone due upon receipt of a "final Clinical Study Report" for "a pharmacokinetic study" determining that "delivery of LEO Pharma's Drug via [Portal's] Device is *bioequivalent* to delivery via a needle/syringe" and including "a statement that the *bioequivalence criteria* have been met" (the "Milestone"). Portal alleges that a "DRAFT" report dated June 15, 2021 (the "PK Phase Report") that does not state anything about bioequivalence triggered this Milestone. Portal also claims that LEO breached the implied covenant of good faith and fair dealing by designing the pharmacokinetics study underlying that report (the "PK Study") and concluding that the PK Study results did not trigger the Milestone.

To assist the trier of fact in evaluating whether the bioequivalence Milestone was triggered and whether LEO acted in good faith in connection with the PK Study, LEO offered Dr. Umesh Banakar as an expert witness. Dr. Banakar is one of the leading experts in the world on the topic of bioequivalence and bioequivalence studies. Throughout his more than 35-year career, he has participated in over a thousand bioequivalence studies involving a variety of study designs. He has written regulatory guidance, textbooks, and other publications on bioequivalence, and taught classes and delivered presentations regarding bioequivalence issues around the world. And he has been qualified as an expert by numerous courts, including on issues relating to bioequivalence.

Dr. Banakar opines that, in order to make a finding of bioequivalence, there must be an assessment of the study data to determine whether the bioavailabilities (i.e., the rate and extent of absorption of the active ingredient) of a test product and a reference produce are, in fact,

equivalent. Dr. Banakar explains that the generally accepted approach for making this assessment—including, *but not limited to*, by regulators around the world—is a 90% confidence interval between 80% and 125% (i.e., that there is a 90% probability that the mean values for the rate and extent of absorption of the test product and reference product are between 80% and 125% of each other). Dr. Banakar also opines that the PK Study used a standard and reasonable design, that the PK Phase Report did not make any statement or determination of bioequivalence, and that LEO correctly concluded that the PK Study did not demonstrate bioequivalence because the results were too variable and fell outside the confidence interval. Dr. Banakar's opinion disproves Portal's claims that the PK Study demonstrated bioequivalence and that LEO acted in bad faith by finding otherwise and helping to design the PK Study.

In an effort to avoid Dr. Banakar's opinion at trial, Portal filed the instant motion to preclude Dr. Banakar from testifying. Portal's motion makes two arguments: (1) that Dr. Banakar purportedly applies an "irrelevant" standard by adopting the confidence interval approach employed by the world's leading drug regulators and public health authority—the U.S. Food and Drug Administration ("FDA"), the European Medicines Authority ("EMA") and the World Health Organization ("WHO"); and (2) that Dr. Banakar purportedly "cherry picks" regulatory guidance by adopting the confidence interval approach of these regulators while allegedly ignoring other aspects of the guidance. Neither argument has any merit.

As to the first argument, Dr. Banakar's testimony is plainly relevant because it will assist the trier of fact in evaluating Portal's remaining claims. Portal argues that Dr. Banakar's approach for determining bioequivalence is purportedly based on an "irrelevant" standard set by regulators. But Portal has conceded throughout this litigation that the way regulatory authorities determine bioequivalence is relevant, including in: (1) Portal's own Complaint which cites to

"*FDA guidance*" regarding specifications for "pass[ing] a bioequivalence test"; (2) the Rule 30(b)(6) deposition of Portal's corporate representative, who testified that Portal's interpretation of the Milestone's "bioequivalence criteria" is based on the criteria "set by … *various bodies, from FDA to WHO*"; and (3) the opening report of Portal's own expert, which explicitly relied on the bioequivalence "definitions set forth by the *FDA and WHO*." Having repeatedly relied on these authorities' interpretations of bioequivalence to advance its own position, Portal cannot exclude Dr. Banakar's testimony for opining on the same subject.

Moreover, Portal's entire argument is premised on a mischaracterization of Dr. Banakar's opinion. As Dr. Banakar has explained, the reason this confidence interval approach applies is not merely that it is the approach adopted by the FDA, EMA, WHO, and other authorities but rather that it is the commonly accepted method—indeed, the *only* commonly accepted method—for determining bioequivalence. Indeed, this confidence interval approach is recognized by the FDA as the "*best available method* for evaluating bioequivalence study data." Academic articles similarly recognize this approach as the "standard" approach to bioequivalence assessments. It is hard to imagine what could be more relevant in a dispute about bioequivalence than the bioequivalence standard commonly accepted in the industry and by the world's leading regulatory bodies. The standard is plainly relevant to the key issues remaining in dispute: whether the PK Study met the Milestone's "bioequivalence criteria" and whether LEO breached the implied covenant by concluding it did not.

As for the second argument, Dr. Banakar's methodology is reliable and not "cherry picked." Portal again misrepresents Dr. Banakar's opinion as stating that the PK Study was required to comply with one aspect of regulatory but permitted to ignore all other aspects. As explained above, Dr. Banakar does not opine that the confidence interval approach applies

because it is "mandated" by regulators, but rather because it is the commonly accepted approach for determining bioequivalence—not just by regulators, but by everyone. Indeed, *even Portal's own expert admits that he has never participated in a study specifically finding bioequivalence without a confidence interval determination*. Nor does Dr. Banakar "disregard" other aspects of regulatory guidance, as Portal argues. He addressed them in his report and at deposition, and a review of that guidance demonstrates that it is either inapplicable or not inconsistent with the PK Study design. Finally, even assuming that Portal's cherry-picking criticism had some merit (and it does not), Portal's quibbles about the PK Study's compliance with technical regulatory guidance at most go to weight of Dr. Banakar's opinion, and not its admissibility.

For these reasons and the reasons below, Portal's motion should be denied.

BACKGROUND

A. Portal's Claim for the Bioequivalence Milestone

This is a breach of contract case arising from a Collaboration and License Agreement (the "Agreement") between LEO and Portal for the development of a needle-free injection system to be used with LEO's drug, tralokinumab. Under the Agreement, LEO had the right to elect whether to develop a single-injection system (the "1x2mL System"), a double-injection system (the "2x1mL System"), or both systems. Agreement (ECF No. 30-1) § 4.2. In exchange for Portal's assistance in development, LEO agreed to make certain payments to Portal, including a $12 million upfront payment and a development fee installment payments while development was ongoing. *Id.* §§ 7.1, 7.2. LEO also agreed to pay Portal milestone payments upon the achievement of milestones defined in the Agreement. *Id.* § 7.3. Portal's remaining claims assert that LEO is required to pay the first of these milestone payments, which is triggered upon:

> Completion of a pharmacokinetic study in animals in which a Third Party determines that delivery of LEO Pharma's Drug via the Device is bioequivalent

> to delivery via a needle/syringe; the date of such completion being the date on which such Third Party provides the final Clinical Study Report to LEO Pharma, which shall include a statement that the bioequivalence criteria have been met and descriptions of attainment of pharmacokinetic endpoints and such safety experience as may have been observed.

Id. The Agreement does not define "bioequivalence" or "bioequivalence criteria."

After executing the Agreement, LEO engaged a leading third-party laboratory (Charles River Laboratories) to conduct the PK Study—an animal pharmacokinetic study of the 2x1mL System. Portal asserts, without any support, that the PK Study "merely served to determine whether [the] commercial milestone was met," even though the stated objective of the study is not commercial or contractual; it is scientific: "to investigate the pharmacokinetics and local tolerance of tralokinumab when dosed [with the 2x1mL System] and [a] prefilled syringe." Protocol (ECF No. 71-5), -659.

Representatives from LEO and Portal engaged in several discussions about the design of this study, including the weights of the animals, the parameters being measured, and the number of subjects. In November 2020, the PK study commenced. *See id.* The PK Study was structured using a "parallel" design in which two groups of 6 pigs each were injected with tralokinumab, one group using the 2x1mL System, and the other group using a traditional pre-filled syringe. *See id.* at -670. During the study, one of the animals needed to be euthanized early after developing a leg injury unrelated to the study.

In or around August 2021, LEO received a "Study Phase" report for the PK Study—the "PK Phase Report." (ECF No. 71-4). The PK Phase Report included a signature but was labelled as "DRAFT." *Id.* at 9. The PK Phase Report did not state anything about bioequivalence—indeed, it nowhere contains the terms "bioequivalence" or "bioequivalent." LEO nonetheless proceeded to analyze the PK Study results to determine whether the data demonstrated bioequivalence. *See, e.g.*, ECF No. 71-3, -940-42. In making that determination, LEO applied the

well-accepted standard for evaluating bioequivalence that is generally applied in the industry and consistently endorsed by global regulators—whether the observed values for rate of absorption (C_{max}) and extent of drug availability (AUC) met a 90% confidence interval between 80% and 125% (or in simpler terms, whether there was a 90% likelihood that the mean values of AUC and C_{max} for Portal's system fall between 80% and 125% of the mean values of those parameters for a pre-filled syringe). *See id.* Applying this standard, LEO determined, consistent with the absence of any statement in the PK Phase Report about bioequivalence, that the PK Study data did *not* demonstrate bioequivalence because the AUC for the 2x1mL System fell outside the confidence interval. *See id.* Accordingly, the Milestone could not have been triggered.

After LEO informed Portal of this conclusion, Portal filed this action asserting that LEO breached the Agreement and the implied covenant of good faith and fair dealing by not paying Portal the $1 million Milestone in response to the PK Study.[1] As LEO will show at trial, Portal cannot recover the Milestone payment for multiple independent reasons, including (but not limited to): (1) the PK Phase Report did not include any "statement that the bioequivalence criteria have been met," as required to trigger the Milestone; (2) the PK Phase Report is not the "final Clinical Study Report" because it was neither the "final" report nor the full "Study Report"; and (3) LEO correctly and reasonably determined that the results of the PK Study did not demonstrate bioequivalence. LEO will further show that it acted in good faith in designing the PK Study, the PK Study design was reasonable, and that Portal was made aware of, and consented or acquiesced to, the key features of the design.

[1] Portal also claimed that LEO breached the Agreement by not paying a $1.5 million development fee relating to the 1x2mL System. On July 20, 2023, the Court granted LEO's motion to dismiss this claim, and on December 8, 2023, the Court denied Portal's request to reconsider that ruling. ECF Nos. 52, 68.

B. Dr. Banakar's Unassailable Qualifications as an Expert

This motion concerns LEO's expert, Dr. Umesh Banakar, who will testify on topics relating to bioequivalence and study design. As Portal does not dispute, Dr. Banakar is well-qualified to offer opinions on these topics as one of the leading experts in the world on bioequivalence and bioequivalence studies.

Dr. Banakar has over 35 years of experience studying, working on, and writing about the issue of bioequivalence. Banakar Rep. (ECF No. 71-7) ¶ 1. He received his Ph.D. in Pharmaceutical Technology from Bombay University in India. *Id.* ¶ 2. After his Ph.D., Dr. Banakar worked as a professor in pharmaceutical sciences, including at Creighton University and Butler University, and developed and taught more than 30 courses on bioequivalence and related subjects. *Id.*, Appx. A; Banakar Tr. (ECF Nos. 71.8-71.9) 24:9-15. He has authored over 300 publications, including a textbook relating to bioequivalence titled "Pharmaceutical Dissolution Testing, Bioavailability and Bioequivalence." Banakar Rep. ¶ 10, Appx. A. He has given presentations regarding bioequivalence issues around the world. *Id.* ¶ 14.

Dr. Banakar has worked in the pharmaceutical industry throughout his career. *Id.* ¶ 3. He is the founder of two Contract Research Organizations—organizations, like Charles River Laboratories, which conduct bioequivalence and other studies on behalf of pharmaceutical and medical device companies—and served on the scientific advisory board of three others. *Id.* ¶ 12. Through this and other work in the industry, he has participated in over a thousand bioequivalence studies, including studies designed for regulatory submission and studies that are not, and involving both animal and human subjects. Banakar Tr. 19:13-22; 101:5-102:17.

Dr. Banakar has extensive experience studying and working with bioequivalence regulatory guidance. As a leading expert in the field, Dr. Banakar helped write the

bioequivalence guidance used by certain countries, including India, Brazil, and Thailand. *See id*. 16:5-9. He also works as a consultant for FDA reviewing drug submissions. Banakar Rep. ¶ 9.

Dr. Banakar has testified and been admitted as an expert in numerous cases, including in cases where he has offered opinions relating to bioequivalence. *See* Banakar Tr. 73:7-18; *see also, e.g.*, *UCB, Inc. v. Teva Pharms. USA, Inc.*, 2015 WL 11199058, at *5 (N.D. Ga. Mar. 18, 2015) (denying motion to exclude Dr. Banakar); *Glaxo Wellcome, Inc. v. Andrx Pharms., Inc.*, 2002 WL 34407982, at *2 (S.D. Fla. Feb. 27, 2002) (same); *Takeda Pharm. Co. Ltd. v. Norwich Pharms., Inc.*, 2022 WL 17959811, at *7 (D.N.J. Dec. 27, 2022) ("Dr. Banakar was admitted as an expert in the fields of pharmacokinetics, dosage form design, and drug product development and evaluation."); *Purdue Pharm. Prod. L.P. v. Actavis Elizabeth LLC*, 2015 WL 5032650, at *9 (D.N.J. Aug. 25, 2015) ("Dr. Banakar was proffered and accepted by the Court as an expert in the field of pharmaceutical formulations."). No court has ever excluded his testimony.

Dr. Banakar's qualifications are a stark contrast to those of Portal's expert, Dr. Uri Herzberg, a consultant who previously worked in the pharmaceutical industry. Dr. Herzberg has only participated in between 12 and 40 bioequivalence studies in his career. Ex. 2, Herzberg Tr. 53:13-54:7. He has never been retained (let alone qualified) as an expert witness. *Id.* 22:11-23:12. He has never published anything on bioequivalence or on designing bioequivalence studies. *Id.* 61:7-62:16. He lacks expertise with bioequivalence regulatory guidance outside the U.S., such as EMA guidance. *Id.* 26:9-22, 299:18-300:15. And Dr. Herzberg is engaged as a paid consultant to Portal on unrelated matters, calling into question his ability to offer an independent and objective opinion as an expert witness. *See id.* 11:15-16:24.

C. The Parties' Respective Expert Opinions

Portal served the expert report of Dr. Herzberg on September 15, 2023. Ex. 3, Herzberg Rep. In his opening report, Dr. Herzberg opined that "the PK Study data demonstrated that, based on definitions set forth by the FDA and WHO, as well as the common scientific understanding of 'bioequivalence,' the two modes of drug administration [i.e., the 2x1mL System and the pre-filled syringe] are bioequivalent" and that LEO's conclusion that the Study did not demonstrate bioequivalence was "inappropriate." *Id.* ¶¶ 40-54. Dr. Herzberg also opined that the PK Study design was "underpowered," including because it did not use a crossover design as recommended by "organizations that publish guidelines on bioequivalence studies, including the European Medicines Association and the FDA." *Id.* ¶¶ 28, 32.

In response, LEO served Dr. Banakar's expert report, which included five principal opinions. First, Dr. Banakar explained that a finding of bioequivalence generally requires a determination that there is a 90% confidence interval of 80% to 125%. Banakar Rep. ¶¶ 22-30. As Dr. Banakar explained, this confidence interval approach "is generally accepted for bioequivalence studies, including by the FDA." *Id.* ¶ 28. Indeed, a statistical confidence interval "is critical to ensure the reliability of bioequivalence studies" by confirming that a bioequivalence finding is adequately robust, precise, and objective. *Id.* ¶ 27. Second, Dr. Banakar opined that the PK Study had a standard and reasonable design, including a discussion of FDA and EMA guidance. *Id.* ¶¶ 31-44. Third, Dr. Banakar found that the PK Phase Report did not make any determination of bioequivalence or include any statement of bioequivalence. *Id.* ¶¶ 45-54. Dr. Banakar opined that the PK Phase Report was insufficient to demonstrate bioequivalence, regardless of whether a confidence interval approach is applied. *Id.* ¶ 53. Fifth, Dr. Banakar conducted an independent review of the PK Study data and concluded that LEO had correctly

determined that it did not demonstrate bioequivalence based on the accepted confidence interval approach. *Id.* ¶¶ 55-62.

On October 20, 2023, Portal served Dr. Herzberg's rebuttal report. In his rebuttal report, Dr. Herzberg abandoned his earlier claim that the PK Study demonstrated bioequivalence "based on definitions set forth by the FDA and WHO …." Ex. 3, Herzberg Rep. ¶ 38. Instead, Dr. Herzberg argued that references to regulatory criteria are "inapposite" and that the relevant criteria was the "ordinary meaning of the term of bioequivalence." Ex. 4, Herzberg Rebuttal ¶¶ 31, 109. Confusingly, however, Dr. Herzberg continued to rely on WHO guidance for a definition of bioequivalence. *Id.* ¶ 30. Dr. Herzberg also criticized the PK Study's design based on regulatory guidance, arguing (for example) that it was inappropriate to use a parallel design because FDA, EMA, and WHO guidance advocates for a crossover design and that the study had too few subjects in light of regulatory guidance. *See, e.g.*, *id.* ¶¶ 48-55, 61-72.

D. Portal's Motion to Preclude Dr. Banakar's Testimony

On December 14, 2023, Portal filed the instant motion to exclude Dr. Banakar. Portal does not argue that Dr. Banakar is unqualified. Nor does Portal identify any purported deficiencies in Dr. Banakar's opinions that the PK Study had a standard and reasonable design, the PK Phase Report did not make any determination or statement of bioequivalence regardless of whether a confidence interval is applied, and LEO accurately performed its statistical analysis. Instead, Portal argues that Dr. Banakar's opinion that bioequivalence should be determined based on a 90% confidence interval must be excluded because, according to Portal, Dr. Banakar (i) applied an "irrelevant" standard based on regulatory guidance that Portal claims is inapplicable, and (ii) "cherry picked" regulatory guidance for demonstrating bioequivalence. As explained below, Portal's criticisms are without merit and do not justify exclusion of Dr. Banakar.

ARGUMENT

Under Federal Rule of Evidence 702, "[a] witness who is qualified as an expert … may testify in the form of an opinion or otherwise if the proponent demonstrates to the court that it is more likely than not that: (a) the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue; (b) the testimony is based on sufficient facts or data; (c) the testimony is the product of reliable principles and methods; and (d) the expert's opinion reflects a reliable application of the principles and methods to the facts of the case."

"It is a well-accepted principle that Rule 702 embodies a liberal standard of admissibility for expert opinions." *Nimely v. City of New York*, 414 F.3d 381, 395 (2d Cir. 2005). Exclusion of expert testimony is "the exception rather than the rule." *Media Glow Digit., LLC v. Panasonic Corp. of N. Am.*, 2019 WL 1055527, at *1 (S.D.N.Y. Mar. 6, 2019) (quoting Fed. R. Evid. 702, Advisory Committee's Notes (2000)). The Court's analysis under Rule 702 "must focus on the principles and methodology employed by the expert, without regard to the conclusions the expert has reached or the district court's belief as to the correctness of those conclusions." *Amorgianos v. Nat'l R.R. Passenger Corp.*, 303 F.3d 256, 266 (2d Cir. 2002).

Where, as here, the Court will serve as the factfinder at trial,[2] "expert testimony should [generally] be admitted so that the Court could have the benefit of live testimony and cross-examination to determine how much weight, if any, to give to the expert's conclusions." *In re Manhattan by Sail, Inc.*, 436 F. Supp. 3d 803, 810 (S.D.N.Y. 2020); *see also Victoria's Secret Stores Brand Management, Inc. v. Sexy Hair Concepts, LLC*, 2009 WL 959775, at *6 n.3

[2] In the Agreement, the parties agreed to "irrevocably waive[] any and all right to trial by jury in any legal proceeding arising out of or related to this Agreement." Agreement (ECF No. 30-1) § 19.11(d). That jury waiver remains in force, and its enforcement has not been waived by LEO. *See id.* § 19.7. Portal's claims must therefore proceed by bench trial.

(S.D.N.Y. Apr. 8, 2009) ("[W]here a bench trial is in prospect, resolving *Daubert* questions at a pretrial stage is generally less efficient than simply hearing the evidence."). Simply put, "there is no need for the Court to 'gate-keep expert testimony from [itself].'" *In re Manhattan*, 436 F. Supp. at 810; *see also Bic Corp. v. Far E. Source Corp.*, 23 F. App'x 36, 39 (2d Cir. 2001) ("[T]he admission of evidence in a bench trial is rarely ground for reversal, for the trial judge is presumed to be able to exclude improper inferences from his or her own decisional analysis.").[3]

I. Dr. Banakar's Opinion that the PK Study Did Not Demonstrate Bioequivalence Is Relevant to Portal's Claims for the Bioequivalence Milestone.

Portal asserts that Dr. Banakar's opinion should be excluded because he allegedly employs an "irrelevant standard of bioequivalence for regulatory approval." To be admissible, an expert opinion must be more likely than not to "help the trier of fact to understand the evidence or to determine a fact in issue." Fed. R. Evid. 702. This relevance requirement, sometimes referred to as a question of "fit," "is satisfied if the expert's opinion would assist the jury's decision on a relevant question of fact without usurp[ing] either the role of the trial judge in instructing the jury as to the applicable law or the role of the jury in applying that law to the facts before it." *United States v. Maxwell*, 2021 WL 5283951, at *5 (S.D.N.Y. Nov. 11, 2021). The relevance requirement is a "low bar." *United States v. Jones*, 2018 WL 1115778, at *9 (S.D.N.Y. Feb. 27, 2018). Any "[d]oubts about whether an expert's testimony will be useful should generally be resolved in favor of admissibility." *Pearlman v. Cablevision Sys. Corp.*, 2015 WL 9462104, at *8 (E.D.N.Y. Dec. 28, 2015).

As explained below, Dr. Banakar's opinion easily clears the low bar of relevance for several reasons, including that: (A) Portal has repeatedly conceded the relevance of regulatory

[3] In light of the Court's role as a factfinder in this case, LEO has not filed a motion to exclude Portal's expert, Dr. Herzberg, notwithstanding serious concerns about his qualifications and opinions. LEO reserves the right to make such a motion at trial or prior to trial.

standards for determining bioequivalence; (B) Portal's argument is premised on a mischaracterization of Dr. Banakar's opinion; and (C) Dr. Banakar's opinion will assist the trier of fact in evaluating both Portal's claim for breach of contract and, independently, its claim for breach of the implied covenant of good faith and fair dealing.

A. Portal Has Conceded the Relevance of Regulatory Standards for Evaluating Bioequivalence.

Portal has repeatedly conceded that the regulatory standard for assessing bioequivalence is relevant—if not controlling—in this this action. For example:

- Portal's Complaint relies on "FDA guidance" regarding the requirements for "pass[ing] a bioequivalence test" and the design of bioequivalence studies. Compl. ¶¶ 44, 58.
- Portal's Rule 30(b)(6) representative testified that Portal's interpretation of "bioequivalence criteria" in the Milestone is based on what is "commonly used in the industry, and … ***set by … various bodies, from FDA to the WHO***." Ex. 1, Portal 30(b)(6) Tr. at 51:2-4 (emphasis added).
- Dr. Herzberg's opening expert report explicitly relied on the FDA and WHO interpretation of bioequivalence and cited FDA, EMA, and WHO guidance. Ex. 3, Herzberg Rep. ¶¶ 17, 28, 38, 42. It was not until Dr. Herzberg's rebuttal report in response to Dr. Banakar's opinion that he shifted his theory to rely on a nebulous "ordinary meaning of the term of bioequivalence" that purportedly differed from the regulatory standard, which Dr. Herzberg labeled "bioequivalence-plus" (a term that does appear in any publication or guidance). *See* Ex. 4, Herzberg Rebuttal ¶ 31.

Given Portal's repeated attempts to rely on the regulatory interpretation of bioequivalence throughout this action, Portal cannot seek to exclude LEO's reliance on that same interpretation merely because it has exposed the flaws in Portal's theory.

B. Portal Mischaracterizes Dr. Banakar's Opinion, Which Follows the Generally Accepted Standard for Evaluating Bioequivalence.

Portal's argument is based on a fundamental distortion of Dr. Banakar's opinion and the established standard for determining bioequivalence. Contrary to Portal's argument, Dr. Banakar's opinion that bioequivalence generally requires a 90% confidence interval between 80% and 125% is *not* simply based on the fact that regulators have uniformly adopted this standard. Rather, as Dr. Banakar explained, the term "bioequivalence" itself "requires some measurement of confidence that … these two ... treatments [or delivery modes] … that we are comparing are equivalent." Banakar Tr. 70:14-20. To determine whether they are equivalent, "I have to have some basis to hang my hat on, and that some basis has to be quantitative." *Id.* 254:23-24; *see also id.* 166:20-21 ("Equivalence is a mathematical determination or a statistical determination."); *id.* 177:14-15 ("[E]quivalent requires some kind of a quantitative assessment."). Without such a calculation, the "study would be just looking at two evaluations without determining bioequivalence." *Id.* 237:21-23.

As Dr. Banakar testified, the 90% confidence interval approach between 80% and 125% "is the generally-accepted way to do it [i.e., determine equivalence], which has a regulatory backing." *Id.* 238:16-17; *see also* Banakar Rep. ¶ 28 ("A 90% confidence interval of 80% to 125% is generally accepted for bioequivalence studies."). In addition to being endorsed by "regulatory agencies worldwide," the confidence interval approach has been the accepted standard in the industry for more than 30 years. Banakar Tr. 239:9-241:4, 254:16-255:5.

This is not merely Dr. Banakar's opinion—which is informed by more than 35 years of experience conducting bioequivalence studies and understanding of industry practice. *See id.* 240:17-241:4. As the FDA explains in adopting this standard, the 90% confidence interval approach is grounded in academic research dating back to the 1980s and is recognized "as the

best available method for evaluating bioequivalence study data."[4] Academic articles similarly recognize that the 90% confidence interval approach is "[t]he standard approach to bioequivalence assessment," the "currently accepted statistical method for declaring bioequivalence," "the most appropriate test," and "proven … under strict scrutiny over more than 20 years."[5] Indeed, *even Portal's own expert*, Dr. Herzberg, admitted at his deposition that he has never "been involved in a study that specifically determined bioequivalence without a confidence interval determination" and that using a confidence interval "is the most common way to determine bioequivalence." Ex. 2, Herzberg Tr. 56:13-19, 229:18-24.

Portal completely fails to rebut this justification for the confidence interval approach in its motion, and instead narrowly and misleadingly focuses on the fact that it is the approach adopted by regulators. Nor does Portal provide any legitimate or reliable alternative to the confidence interval approach.

Instead, Portal asserts that a one-sentence general definition purportedly from a 1985 "Illustrated Medical Dictionary" is the relevant one, even though Portal's own expert did not cite to that definition in either of his two reports.[6] But even assuming that definition is applicable here, it merely begs the question of *how* to determine whether two treatments "hav[e] the same strength and similar bioavailability." *See* Banakar Tr. 165:20-166:10 (explaining that a general

[4] CVM Guidance (ECF No. 71-11), at 17 (emphasis added).

[5] Hsing-Chu Hsu, et al., *A Comparative Study of Confidence Interval and Confidence Region Methods in Determination of Bioequivalence between Two Formulations*, 29 Drug Information Journal 1021-1028, 1021-22 (1995); Richard Schall, *Bioequivalence: tried and tested*, 21 Cardiovascular J. of Africa 69-71, 70-71 (Mar./Apr. 2010).

[6] It appears that the 1985 22nd edition of Dorland's Illustrated Medical Dictionary cited by Portal does not exist, as the 23rd edition was first published in 1957. *See* Library of Congress Catalog, Dorland's Illustrated Medical Dictionary, https://lccn.loc.gov/00006383. We assume this is an inadvertent miscitation, but it underscores the fundamental lack of rigor in Portal's proposed approach to evaluating bioequivalence.

definition of bioequivalence simply leads to the question "How do I determine bioequivalence?"). The same is true of the general FDA and WHO definitions cited by Portal: they do not explain *how* to determine whether the rate and extent of availability are sufficiently "similar" in order to be "bioequivalent." As Dr. Banakar opines, the well-established 90% confidence interval between 80% and 125% provides the answer.

Dr. Herzberg similarly fails to provide any reliable alternative to the confidence interval approach. In contrast to Dr. Banakar's approach, which has been universally adopted by regulators and recognized by the FDA "as the best available method for evaluating bioequivalence study data," CVM Guidance at 17, Dr. Herzberg proposes determining bioequivalence by asking whether it "walks and talks and barks like bioequival[ence]"—an approach which Dr. Herzberg was unable to support by reference to any academic or regulatory literature. Ex. 2, Herzberg Tr. 105:13-106:4, 366:17-368:22.

At most, Portal's argument merely shows that Dr. Banakar and Dr. Herzberg have a difference of opinion as to the appropriate method for determining bioequivalence. But the fact that Dr. Banakar offers a "competing analysis" within the same subject matter as Dr. Herzberg provides no basis for exclusion. *See Capri Sun GmbH v. Am. Beverage Corp.*, 595 F. Supp. 3d 83, 140–41 (S.D.N.Y. 2022) (rejecting argument to exclude expert who allegedly "reli[ed] on a flawed competing methodology" because it would "read[] *Daubert*'s 'fit' requirement too narrowly," and noting that the expert's opinion was "not out of bounds on account of its different, and more demanding, methodology"). Portal's argument is contrary to the well-settled rule that a court "should not arrogate the [factfinder's] role in evaluating the evidence and the credibility of expert witnesses by simply choosing sides in the battle of the experts." *In re Joint E & S Dist. Asbestos Lit.*, 52 F.3d 1124, 1135 (2d Cir. 1995) (alteration marks omitted).

C. Dr. Banakar's Opinion Will Assist the Trier of Fact in Deciding Portal's Claims.

The evidence in this case demonstrates that Dr. Banakar's opinion is relevant to both of Portal's remaining claims.

First, Dr. Banakar's opinion will assist the factfinder in deciding Portal's breach of contract claim by showing, consistent with the lack of any explicit finding of bioequivalence in the PK Phase Report, that the PK Study did not demonstrate that delivery via Portal's device was "bioequivalent" to delivery through a syringe, and thus did not trigger the Milestone. *See* Compl. ¶¶ 46-60. Where, as here, parties to an agreement use a technical term like "bioequivalence," "courts may consider evidence regarding the technical meaning of that term in the industry in question even without a threshold finding that the contract is ambiguous." *Pujals v. Standard Chartered Bank*, 533 F. App'x 7, 10 (2d Cir. 2013). As Dr. Banakar and other witnesses can testify, bioequivalence is understood in the pharmaceutical and medical device industry as involving the same confidence interval approach endorsed by FDA and other regulators around the world. *See, e.g.*, Banakar Tr. 238:16-17; 240:20-24, 254:16-255:5. Indeed, Portal's Rule 30(b)(6) representative admitted that the meaning of "bioequivalence" in the Milestone is based on what is "commonly used in the industry and … set by … ***various bodies, from FDA to the WHO***." Ex. 1, Portal 30(b)(6) Tr. at 51:2-4 (emphasis added).

To the extent that Portal now intends to reverse its prior position and argue that the bioequivalence Milestone should not be interpreted by reference to the industry and regulatory standard, that provides no basis for excluding Dr. Banakar. "[T]he testimony of a party's expert must be evaluated within the context of that party's own theory of the case." *Olin Corp. v. Lamorak Ins. Co.*, 2018 WL 1901634, at *21 (S.D.N.Y. Apr. 18, 2018). Because "the legal or factual sustainability of [LEO's] theory has not yet been decided," an argument that the theory

"may be legally or factually deficient is not justifications for concluding that … the expert's testimony is unreliable or unhelpful." *Sec. & Exch. Comm'n v. Ripple Labs, Inc.*, 2023 WL 5670711, at *18 (S.D.N.Y. Mar. 6, 2023).

Second, Dr. Banakar's opinion is also independently relevant to Portal's claim that LEO breached the implied covenant of good faith and fair dealing by conducting a statistical analysis of the PK Study. *See* Compl. ¶¶ 52-53, 57-59, 80. In order to demonstrate a breach of the implied covenant, "[a] plaintiff must show substantially more than evidence that the defendant's actions were negligent or inept," "such as that the defendant 'act[ed] arbitrarily or irrationally in exercising the discretion' afforded to it under the contract." *N. Am. Photon Infotech Ltd. v. ZoomInfo LLC*, 2021 WL 4482208, at *5 (S.D.N.Y. Sept. 30, 2021). "Courts applying New York law 'generally hold that a defendant violates the covenant of good faith and fair dealing only when he acts with some improper motive.'" *Wagner v. JP Morgan Chase Bank*, 2011 WL 856262, at *4 (S.D.N.Y. Mar. 9, 2011).

Dr. Banakar's opinion that LEO correctly applied a 90% confidence interval standard in evaluating bioequivalence, consistent with the generally accepted approach, demonstrates that LEO's analysis of the study results was in good faith and not arbitrary, irrational, or the result of improper motive. As LEO's 30(b)(6) representative testified at deposition, LEO analyzed the PK Study results using a 90% confidence interval because "where you want to claim bioequivalence, you need to fulfill the bioequivalence criterion, which is that the 90 percent confidence interval is between 0.8 and 1.25 of the geometric mean ratios for AUC and [C_{max}]." LEO 30(b)(6) Tr. (ECF No. 71-10) 137:17-22. Thus, at a minimum, Dr. Banakar's opinion will assist the factfinder by explaining the basis and context for LEO's confidence interval analysis. *See* Fed. R. Evid. 702 (expert testimony admissible when it "help the trier of fact to understand the evidence"); *see also*

Ripple Labs, 2023 WL 5670711, at *6 (an expert "need not directly address the central issue in the case to be relevant; the proper question is 'whether the expert's testimony as to a particular matter will assist the trier of fact'").

II. Dr. Banakar Applies a Reliable Methodology.

Portal next argues that Dr. Banakar's opinion is unreliable because it purportedly "cherry picks" portions of regulatory guidance. An expert's testimony is reliable if it has "a reliable basis in the knowledge and experience of his discipline." *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 149 (1999). Under Rule 702, "only serious flaws in reasoning or methodology will warrant exclusion." *In re Fosamax Prods. Liab. Litig.*, 645 F. Supp. 2d 164, 173 (S.D.N.Y. 2009). Other deficiencies in an expert's opinion go to the testimony's weight, not its admissibility. *Zerega Ave. Realty Corp. v. Hornbeck Offshore Transp., LLC*, 571 F.3d 206, 214 (2d Cir. 2009). For example, "the existence or number of supporting authorities for an opinion speak to the weight of an expert's opinion, not its admissibility." *Ripple Labs*, 2023 WL 5670711, at *10. Similarly, the "mere fact that an expert's testimony conflicts with the testimony of another expert or scientific study does not control admissibility." *In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d 230, 285 (E.D.N.Y. 2007). Unless expert testimony "is speculative or conjectural or based on assumptions that are 'so unrealistic and contradictory as to suggest bad faith or to be in essence an apples and oranges comparison,'" it should not be excluded as unreliable. *Zerega*, 571 F.3d at 214. Portal fails to identify any flaws in Dr. Banakar's reasoning or methodology warranting exclusion.

A. Portal's Cherry Picking Argument Mischaracterizes Dr. Banakar's Opinion.

To begin with, Portal's argument is once again premised on a distortion of Dr. Banakar's opinion. Dr. Banakar does *not* opine that aspects of regulatory guidelines specifying a 90% confidence interval are "always mandatory" whereas all other aspects of those guidelines are

"optional," as Portal argues. Rather, Dr. Banakar explains that, while regulatory guidelines are by definition non-binding (especially in the context of a non-submission study), the confidence interval approach is the generally accepted approach for determining bioequivalence. *See, e.g.*, Banakar Tr. 216:16-20 ("[T]he only way that is accepted for bi -- bioequivalence for most of the drugs is 90 percent confidence interval for these two parameters."), 297:15, 300:17-21; *see also supra* Part I.B (discussing the basis for and general acceptance of the confidence interval approach). That is a well-reasoned and supported opinion, not cherry picking or *ipse dixit*. *See, e.g.*, *Pearlstein v. Blackberry Ltd.*, 2021 WL 4131646, at *9 (S.D.N.Y. Sept. 10, 2021) (explaining that it is "not 'cherry picking'" to have "[d]ifferences of opinion about what is important" and that criticisms about such differences "go to the weight of the expert's opinion, not an expert's ability to offer that opinion").[7]

Indeed, Portal's "cherry picking" criticism more accurately applies to its own position than to Dr. Banakar's. Portal has relied on FDA and WHO interpretations of bioequivalence when it suits its position (as in Dr. Herzberg's opening report), and dismissed those interpretations as "irrelevant" or "cherry picked" when it doesn't.

B. Portal Fails to Show that the PK Study Was Inconsistent with Relevant Regulatory Guidance.

Portal is also incorrect that Dr. Banakar's opinion "disregards" regulatory guidance regarding study design. In fact, Dr. Banakar's report discusses regulatory guidance regarding the number of subjects (*see, e.g.*, ¶¶ 32-34), the use of a parallel vs. cross-over design (*see, e.g.*,

[7] Portal takes out of context Dr. Banakar's testimony that the 90% confidence interval range has become "mandatory for practice" for submission studies based on the FDA's approval practices. As Dr. Banakar went on to explain (in testimony Portal omits), it is effectively mandatory for non-submission studies because there needs to be a "statistical evaluation … to show that they are … bioequivalent." Banakar Tr. 302:2-7; *see also supra* Part I.B. Moreover, Dr. Banakar noted that there are exceptions to the 90% confidence interval between 80% and 125%, but Portal elected not to explore those exceptions at his deposition. *See* Banakar Tr. 253:13-254:15.

¶¶ 38-39), and the contents of the protocol (*see, e.g.* ¶¶ 37, 42). Portal's disagreement with that analysis does not mean it was cherry picked, let alone so unreliable as to justify exclusion. Far from "cherry picking," a review of regulatory guidance and Dr. Banakar's report and testimony demonstrate that, while the PK Study was not designed nor required to meet any specific regulatory guidance, it was consistent with relevant guidance in all material respects.

Cross-Over vs. Parallel Design. Regulatory guidance makes clear that the PK Study appropriately used a parallel design, as even Portal's own expert now concedes. Although FDA and EMA guidance state that a cross-over design are "commonly used" and generally "recommended," they do not require such a design. CVM Guidance at 14; EMA Guidance (ECF 71-13) at 6. To the contrary, this guidance makes clear that alternative designs, such as a parallel design should be considered depending on the circumstances. CVM Guidance at 15; EMA Guidance at 6. In particular, a parallel design "may be preferable" when (for example) the "duration of the washout time"—i.e., the time it takes to sufficiently clear the drug from the subject's system—for a cross-over study "is so long as to result in significant maturational changes in the study subjects." CVM Guidance at 15.

As Dr. Banakar explained, a parallel design was appropriate for the PK Study because tralokinumab has a long washout period, meaning that it would require several additional months to conduct a cross-over design, during which the study subjects would significantly mature. *See* Banakar Rep. ¶ 39. In fact, Dr. Banakar's opinion that it was appropriate for the PK Study to use a parallel design is so well-supported that *even Portal's own expert was forced to agree with it*. After initially opining that the PK Study should have used a cross-over design, Portal's expert

backtracked at his deposition and conceded that, in light of the necessary washout period, it was appropriate to use a parallel design. Ex. 2, Herzberg Tr. 331:2-7, 410:8-18.[8]

Number of Subjects. The fact that the PK Study used 12 subjects is also supported by regulatory guidance. As Dr. Banakar noted in his report, regulatory guidance states that a minimum of 12 subjects should be included in a bioequivalence study. *See* Banakar Rep. ¶ 32; *see e.g.*, EMA Guidance at 8. Further, since using more than the minimum puts additional animal lives at risk, the EU Directive for the Protection of Animals Used for Scientific Purpose (which LEO, as a European company, follows) provides that animal studies "should use the minimum number of animals that would provide reliable results." Banakar Rep. ¶ 33. That is exactly what was done in the PK Study: The protocol states that the "number of animals chosen for this study are the smallest number considered necessary to provide reliable data." Protocol, -667.

Portal points to regulatory guidance stating that "generally" more subjects are needed in a parallel design than in a cross-over design and recommending the inclusion of subjects to allow for dropouts, but that does not necessarily mean that more than 12 subjects was appropriate (let alone necessary) for the PK Study. The guidance does not set a different minimum number for a parallel design than for a cross-over design. And if it were true that more than 12 subjects is always necessary to allow for dropouts, then there would be no reason for the guidance to set a 12 subject minimum in the first place. Indeed, Portal presents no analysis demonstrating that the dropout risk here was sufficient in order to warrant sacrificing more than 12 animals for the PK Study. Moreover, Dr. Banakar addressed these issues in his report and deposition and explained,

[8] Portal quibbles with Dr. Banakar's statement that, based on his experience, there is a "choice" as to whether to conduct a study in a parallel or crossover manner and that FDA makes "no assumptions" about which design will be carried out. That is entirely consistent with FDA guidance, which states that a parallel design "may be preferable" depending on the circumstances. CVM Guidance at 15.

based on his more than 35 years of experience working with regulators and conducting bioequivalence studies, that 12 subjects can be adequate for a parallel design depending on the details of the study. *See, e.g.*, Banakar Rep. ¶¶ 32, 34-36; Banakar Tr. 279:19-282:9, 287:20-289:12, 323:11-325:13. While Portal and its expert may disagree with Dr. Banakar's analysis, that does not provide any justification for excluding Dr. Banakar's opinion. *See Zyprexa*, 489 F. Supp. 2d at 285 ("The mere fact that an expert's testimony conflicts with the testimony of another expert or scientific study does not control admissibility.").

Protocol Contents. Portal also fails to demonstrate that supposed omissions in the details of the PK Study protocol justify exclusion of Dr. Banakar's opinion. As an initial matter, Portal does not explain why these non-substantive guidelines about what information regulators recommend stating in study protocols submitted to them have any relevance to a study that Portal concedes was not intended for submission. For example, while FDA guidance state that "[t]he sponsor and CVM [FDA Center for Veterinary Medicine] should agree to acceptable bounds for the confidence limits for the particular drug and formulation during protocol development," this recommendation makes no sense when there is no intention to submit the protocol to CVM.

Further, the bulk of Portal's critique is based on WHO guidelines which "provide recommendations to regulatory authorities" concerning "approval of multisource (generic) pharmaceutical products" without showing that this guidance has any application here. ECF No. 71-14, at 184. As Dr. Banakar explained, WHO guidance is used for "countries that don't even have [bioequivalence] regulations." Banakar Tr. 174:13. Dr. Banakar only cited WHO guidance to show that Dr. Herzberg's reliance on that guidance contradicted Dr. Herzberg's position. Banakar Rep. ¶ 30. In contrast, FDA's CVM guidance does not require stating a justification

regarding the number of test subjects, the study design, or the exclusion of data. *See* CVM Guidance.

In addition, as Dr. Banakar explained at his deposition, the recommendations about the contents of a protocol are generally not mandated as a matter of practice, even for submission studies (much less non-submission studies), absent atypical study specifications. *See, e.g.*, Banakar Tr. 226:10-22. Contrary to Portal's argument, this testimony was adequately supported on Dr. Banakar's more than 35 years of experience working with the FDA and other regulators on bioequivalence studies. *Id.* at 210:20-211:15, 224:3-225:18, 228:2-14, 241:5-242:18.

In any event, the key elements of the PK Study's design were specified in the protocol. For example, the protocol included provisions regarding justification of number of animals, the experimental design, and the parameters being estimated. *See* Protocol, -667, -670, -672-75. Even assuming that Portal can show that these provisions were somehow insufficient in the context of a non-submission study, that is not a basis to exclude Dr. Banakar. *See Amorgianos*, 303 F.3d at 267 ("A minor flaw in an expert's reasoning or a slight modification of an otherwise reliable method will not render an expert's opinion per se inadmissible.").

C. Portal's Criticism Goes to Weight and Not Admissibility.

Finally, even assuming Portal's argument had some merit (and it does not), it would go to the *weight* of Dr. Banakar's testimony and not its *admissibility*. At bottom, Portal claims that Dr. Banakar's methodology applies some aspects of regulatory guidance, and not others. But generally "gaps or inconsistencies in the reasoning leading to [the expert's] opinion ... go to the weight of the evidence, not to its admissibility." *Restivo v. Hessemann*, 846 F.3d 547, 577 (2d Cir. 2017). Courts have thus found that cherry-picking arguments similar to Portal's here "are best left for adversarial testing at trial." *Capri Sun*, 595 F. Supp. 3d at 135; *see also, e.g.*, *Sec. &*

Exch. Comm'n v. Laura, 2023 WL 4238153, at *7 (E.D.N.Y. June 28, 2023) ("[E]ven assuming that any of Defendants' objections [regarding cherry picking] are valid, their criticism goes only to the weight of [the expert's] opinion, not its admissibility.").[9]

"Vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence." *Daubert v. Merrell Dow Pharms., Inc.*, 509 U.S. 579, 596 (1993). Portal utterly fails to show that cross-examination and its own expert's contrary opinion are insufficient for the factfinder to evaluate its critique of Dr. Banakar's opinion.

CONCLUSION

For the foregoing reasons, Portal's motion to exclude Dr. Banakar should be denied.[10]

[9] The authority Portal cites is all inapposite. *See, e.g.*, *In re Mirena Ius Levonorgestrel-Related Prod. Liab. Litig. (No. II)*, 341 F. Supp. 3d 213, 297 (S.D.N.Y. 2018) (excluding expert opinion theorizing on model of causation that was "unsound methodologically at nearly each step," untested and unpublished, and "speculative" and "conjectural" by the expert's own admission); *Piepes v. NAI Ent. Holdings LLC*, 394 F. Supp. 3d 315, 319 (E.D.N.Y. 2019) (excluding expert opinion on medical causation because, among other deficiencies, it had "no explanation, citation, or analysis" for his conclusions); *Scentsational Techs., LLC v. Pepsi, Inc.*, 2018 WL 1889763, at *3 (S.D.N.Y. Apr. 18, 2018) (excluding portions of expert opinions relating to food packaging that had "no evidence or support" and were "pure speculation," or were inadmissible factual narratives, descriptions of states of mind, or legal conclusions).

[10] In the event the Court disagrees and is inclined to preclude Dr. Banakar's testimony, the Court's ruling should be limited to the extent Dr. Banakar relies on the 90% confidence interval approach, as Portal does not assert a basis for the exclusion of other aspects of Dr. Banakar's opinion, including that the PK Study was appropriately designed and that, even putting aside the confidence interval, "it cannot be said that the PK Phase Report demonstrates bioequivalence." Banakar Rep. ¶ 53. *See In re Pfizer Sec. Litig.*, 819 F.3d 642, 665 (2d Cir. 2016) ("[W]hen the unreliable portion of an opinion can easily be distinguished from testimony that could help the [factfinder], it may be an abuse of discretion to throw the good out with the bad.").

Respectfully submitted,

New York, New York
Dated: January 19, 2024

COVINGTON & BURLING LLP

/s/ Jordan S. Joachim
Mark P. Gimbel
Jordan S. Joachim
The New York Times Building
620 Eighth Avenue
New York, NY 10018
212-841-1000
mgimbel@cov.com
jjoachim@cov.com

Attorneys for Defendant LEO Pharma A/S